# General

## Guideline Title

ACR Appropriateness Criteria® pretreatment evaluation and follow-up of endometrial cancer.

## Bibliographic Source(s)

Lalwani N, Dubinsky T, Javitt MC, Gaffney DK, Glanc P, Elshaikh MA, Kim YB, Lee LJ, Pannu HK, Royal HD, Shipp TD, Siegel CL, Simpson L, Wahl AO, Wolfson AH, Zelop CM, Expert Panel on Women's Imaging and Radiation Oncology â€“ Gynecology. ACR Appropriateness CriteriaÂ® pretreatment evaluation and follow-up of endometrial cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 12 p. [61 references]

## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Lee J, Dubinsky T, Andreotti RF, Cardenes HR, Allison SO, Gaffney DK, Glanc P, Horowitz NS, Jhingran A, Lee SI, Puthawala AA, Royal HD, Scoutt LM, Small W Jr, Varia MA, Zelop CM, Expert Panel on Women's Imaging and Radiation Oncology - Gynecology. ACR Appropriateness Criteria® pretreatment evaluation and follow-up of endometrial cancer of the uterus. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 9 p.

# Recommendations

## Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Pretreatment Evaluation and Follow-up of Endometrial Cancer

Variant 1: Newly diagnosed endometrial cancer; when imaging is indicated for treatment planning. (See narrative for clinical scenarios where imaging would be indicated.)

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| MRI pelvis without and with contrast | 9 | See statement regarding contrast in text below under "Anticipated Exceptions." | O |
| CT chest with contrast | 7,8,9 Usually appropriate | This procedure is for patients at high risk for metastases. | O |

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| MRI abdomen without and with contrast | 7 | See statement regarding contrast in text below under "Anticipated Exceptions." | O |
| CT abdomen with contrast | 7 | This procedure is used to evaluate for para-aortic lymphadenopathy. | |
| X-ray chest | 7 | This procedure may be appropriate if chest CT is not performed or unavailable. | |
| CT pelvis with contrast | 5 | This procedure may be appropriate if MRI cannot be obtained. | |
| MRI pelvis without contrast | 5 | | O |
| CT chest without contrast | 4 | This procedure is for patients at high risk for metastases. | |
| MRI abdomen without contrast | 4 | | O |
| US pelvis transvaginal | 3 | This procedure may be appropriate if MRI cannot be performed. | O |
| CT abdomen without contrast | 1 | | |
| CT abdomen without and with contrast | 1 | | |
| CT pelvis without contrast | 1 | | |
| CT pelvis without and with contrast | 1 | | |
| CT chest without and with contrast | 1 | This procedure is for patients at high risk for metastases. | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Assessing the depth of myometrial invasion.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| MRI abdomen without and with contrast | 7 | See statement regarding contrast in text below under | O |

| Radiologic Procedure | Rating | Comments "Anticipated Exceptions." | RRL* |
|---|---|---|---|
| US saline infusion sonohysterography | 4 | With this procedure there is very low risk of malignant cell dissemination into peritoneal cavity, which does not alter stage. | O |
| MRI pelvis without contrast | 3 | This procedure is useful if gadolinium is contraindicated. | O |
| CT pelvis with contrast | 3 | | |
| US pelvis transvaginal | 3 | This procedure may be appropriate if MRI cannot be performed. | O |
| CT pelvis without contrast | 1 | | |
| CT pelvis without and with contrast | 1 | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Lymph node evaluation.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| FDG-PET/CT skull base to mid-thigh | 9 | This procedure is appropriate for patients with high-grade tumor(s) that are likely FDG-avid. | |
| CT pelvis with contrast | 8 | | |
| CT abdomen with contrast | 8 | | |
| MRI pelvis without and with contrast | 8 | See statement regarding contrast in text below under "Anticipated Exceptions." | O |
| MRI abdomen without and with contrast | 8 | See statement regarding contrast in the text below under "Anticipated Exceptions." | O |
| MRI pelvis without contrast | 6 | | O |
| MRI abdomen without contrast | 6 | | O |
| CT pelvis without contrast | 5 | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation |

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| CT abdomen without contrast | 4 | | |
| US pelvis transabdominal | 2 | | O |
| CT pelvis without and with contrast | 1 | | |
| CT abdomen without and with contrast | 1 | | |
| Lymphangiogram | 1 | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Assessing endocervical tumor extent.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| MRI pelvis without and with contrast | 9 | See statement regarding contrast in text below under "Anticipated Exceptions." | O |
| MRI pelvis without contrast | 6 | | O |
| US pelvis transvaginal | 4 | This procedure is useful if MRI cannot be performed. | O |
| CT pelvis with contrast | 3 | | |
| CT pelvis without contrast | 1 | | |
| CT pelvis without and with contrast | 1 | | |
| Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate | | | *Relative Radiation Level |

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: Post-therapy evaluation in patients with clinically suspected recurrence.

| Radiologic Procedure | Rating | Comments | RRL* |
|---|---|---|---|
| FDG-PET/CT skull base to mid-thigh | 9 | This procedure is appropriate for patients with high-grade tumor(s) that are likely FDG-avid. | |
| MRI pelvis without and with contrast | 8 | See statement regarding contrast in text below under "Anticipated Exceptions." | O |
| CT pelvis with contrast | 8 | This procedure is appropriate if FDG-PET is not performed. | |
| MRI abdomen without and with contrast | 8 | See statement regarding contrast in text below under "Anticipated Exceptions." | O |
| CT abdomen with contrast | 7 | This procedure is appropriate if FDG-PET or MRI of abdomen is not performed or is unavailable. | |
| MRI pelvis without contrast | 6 | | O |
| MRI abdomen without contrast | 6 | | O |
| CT chest with contrast | 6 | | |
| CT chest without contrast | 4 | | |
| X-ray chest | 4 | This procedure may be appropriate if chest CT and FDG-PET are not performed or are unavailable. | |
| CT pelvis without contrast | 2 | | |
| CT abdomen without contrast | 2 | | |
| CT pelvis without and with contrast | 1 | | |
| CT abdomen without and with contrast | 1 | | |
| CT chest without and with contrast | 1 | | |

| Radiologic Procedure | Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate<br>Rating | Comments | *Relative Radiation Level |
|---|---|---|---|

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Precise pretreatment evaluation of endometrial cancers facilitates an optimized therapeutic approach, particularly with regard to choosing type of surgery. Cross-sectional imaging techniques can play a vital role in pretreatment assessment of uterine cancers and should be viewed as complementary tools for surgical evaluation of these patients. Local-regional invasion of pelvic structures and distant metastasis can be readily detected on routine and standardized radiologic imaging. Although ultrasound (US) remains the primary imaging modality of choice for women who have suspected endometrial carcinoma (EC), state-of-the-art dynamic contrast-enhanced and diffusion-weighted magnetic resonance imaging (MRI) techniques are the primary modalities of choice for women who require preoperative staging EC or an imaging assessment of recurrence or treatment response.

Clinical Background and Prognostic Factors

EC is the most common gynecologic malignancy and the fourth most common cancer in women in the United States. About 47,130 new cases and 8,010 deaths were expected in the United States in 2012.

Histopathologically, the ECs are classified as type I (>80%) and type II (<20%). Type I is typically composed of endometrioid type and estrogen-dependent cancers. They are often low grade, preceded by a premalignant endometrial hyperplasia, and demonstrate better prognosis. Type II is often made up of nonestrogen-dependent, nonendometrioid, and high-grade tumors which arise from an atrophic endometrium. They demonstrate a dismal prognosis and are responsible for almost half of the EC-related deaths.

The surgical and therapeutic strategy may be changed with the International Federation of Gynecology and Obstetrics (FIGO) staging system. A revised simple FIGO staging scheme was approved September 2008. Stage I is defined as a tumor confined to the corpus uteri with or without myometrial invasion. Myometrial invasion <50% is assigned to stage IA and >50% as IB. Stage II signifies tumors invading the cervical stroma (not extending beyond the uterus). Stage III includes local and regional spread of disease and is classified in 3 categories. Tumors invading the serosa or adnexa are assigned stage IIIA, whereas tumors invading the vagina or parametrium are designated with stage IIIB. Presence of positive lymph nodes is assigned with stage IIIC, which is further divided in IIIC1 (positive pelvic nodes) and IIIC2 (positive para-aortic lymph nodes) disease. A tumor invading bladder and/or bowel mucosa is categorized as stage IVA, whereas distant metastasis (e.g., to lung or liver) as IVB.

Endometrial cancer primarily presents at stage I (80% of cases), and the recommended treatment is complete resection of disease, hysterectomy, and bilateral salpingo-oophorectomy. Depending on prognostic factors such as depth of myometrial invasion, tumor size, and tumor grade, lymphadenectomy may also be indicated, though some gynecologic oncologic surgeons believe that lymphadenectomy is indicated in all patients with EC, whereas others do not recommend routine lymphadenectomy in any patient. Once lymph node metastasis is confirmed by histology, adjuvant radiation or chemotherapy could be considered.

The potential advantages of preoperative imaging may include:

1. Evaluation of the depth of myometrial invasion to predict the likelihood of advanced disease (i.e., incidence of lymph node metastasis is <2.5% in stage IA versus 15%–45% in stage IB)
2. Diagnosis of gross cervical invasion, which requires preoperative radiation therapy or a different treatment plan (i.e., radical hysterectomy instead of total abdominal hysterectomy)
3. Identification of suspicious lymph nodes to guide lymph node sampling at the time of surgery
4. Detection of advanced disease

The most important prognostic variables for carcinoma of the uterus are the histologic grade and the stage of tumor, including depth of myometrial invasion and lymph node metastasis. In a study of 349 endometrial cancer patients correlating the incidence of pelvic lymph node metastases with histologic grade and depth of myometrial invasion, lymph node metastases were found in less than 10% of patients with grade 1 and 2 disease with no or inner half (<50%) of myometrial invasion (stage IA) versus 17% with outer half (>50%) of myometrial invasion (stage IB). In histologic grade 3 disease, lymph node metastases were identified in up to 28% of patients with any degree of myometrial invasion (stage IA and IB).

In a study of 200 patients with adenocarcinoma of the uterus, the depth of myometrial invasion was found to be the single most important

prognostic factor. In stage IA disease, when the tumor is confined to the endometrium or to the superficial myometrium, the incidence of para-aortic lymph node metastases was <2.5%. Conversely, in stage IB disease, when there is deep myometrial invasion, para-aortic lymph node metastases occurred in 15% to 5% of patients.

The first-echelon (or efferent) lymph nodes for endometrial cancer include either pelvic or para-aortic nodal stations and are the most at risk. A study of 422 endometrial cancer patients operated on consecutively at a single center demonstrated pelvic and para-aortic metastatic lymphadenopathy in 51% of patients and para-aortic nodal involvement alone in 16% of patients at lymphadenectomy. However, lymphadenectomy does not alter overall survival, especially in early-stage endometrial cancer. Thus, pretreatment lymph node evaluation with imaging should include assessment of pelvic and para-aortic nodes to guide lymph node sampling at the time of surgery.

Because errors in clinical staging are estimated to result in understaging of about 13% to 22% in patients with endometrial cancer, the FIGO has recommended routine surgical staging since 1988. Preoperative imaging of EC can define the extent of disease to tailor treatment and indicate subspecialist referral if deep myometrial invasion, cervical extension, or lymphadenopathy is suspected or if high-grade or high-risk histology (such as papillary serous or clear-cell carcinoma) is found at the time of biopsy. Diagnostic imaging may be helpful in obese, elderly patients in whom radiation therapy rather than surgery might be advocated as the primary treatment or as a preoperative adjuvant to surgery. Imaging may also benefit young women with EC who want to preserve fertility, in which case hormonal therapy would be considered as a primary treatment rather than surgery.

EC tends to recur in the pelvis, especially in the vaginal vault (42% of recurrences) and pelvic lymph nodes, followed by para-aortic lymph nodes. Other common sites for extrapelvic recurrence are the abdomen (especially peritoneum) and lung. Therefore, post-therapy surveillance imaging may include evaluation of the abdomen and pelvis. Imaging of the chest may be indicated in selected high-risk, advanced-stage patients to detect lung metastasis.

Use of Imaging in Clinical Guidelines

*Transabdominal and Transvaginal Ultrasound*

Transabdominal US is considered unreliable in staging endometrial cancer, though its use has shown some promise in evaluating myometrial invasion. Reported accuracies in stage I cancer range from 69% to 93% in differentiating deep invasion (stage IB) from absent or superficial invasion (stages IA). Studies using high-frequency transvaginal US showed similar accuracies ranging from 73% to 84% in assessing myometrial invasion. A study using transvaginal and Doppler US also showed an accuracy of 69% in predicting myometrial invasion. However, studies directly comparing the accuracy of transvaginal US to that of contrast-enhanced MRI for staging have consistently demonstrated that the latter performs with greater accuracy.

In addition, there are insufficient reports about the value of transvaginal US in predicting cervical extension, parametrial invasion, or lymphadenopathy. In 1 study, transvaginal US showed cervical involvement in only 7 of 10 patients with cervical extension. Studies have shown that contrast-enhanced US could be useful to diagnose the depth of myometrial infiltration using the arcuate vascular plexus involvement as a marker; however, this needs further validation.

Hysterosonography (i.e., transvaginal US evaluation of the uterus after intracavitary saline infusion) has been used for evaluating deep myometrial invasion, with accuracies ranging from 84% to 89%. However, its use is controversial in determining the myometrial invasion, and several reports indicated that the procedure can disseminate malignant cells into the peritoneal cavity in 6% to 7% of patients with an established diagnosis of endometrial cancer.

*Computed Tomography*

Computed tomography (CT) has been used for evaluating EC, with emphasis on the depth of myometrial invasion and assessing lymph node status. However, CT is insensitive for depicting endometrial cancer in the uterus and therefore its role in evaluating myometrial invasion is limited. This is particularly true for small and low-risk EC (stage IA or IB). In studies comparing CT with US or MRI, the accuracy of CT for myometrial invasion is reported to be 58% to 61% versus 68% to 69% for US and 88% to 89% for MRI. The value of CT in diagnosing cervical extension is not evident because identifying the margin between the cervix and the uterine corpus is difficult on axial imaging planes. Moreover, most studies suffer from having only a few patients with stage II cancer, which may prevent the drawing of valid conclusions. A recent study in preoperative evaluation of myometrial invasion and cervical extension of endometrial cancer using multidetector CT (MDCT) showed improved diagnostic accuracies of 95% and 81%, respectively. However, the role of MDCT for staging EC must be further validated. For evaluation of pelvic and para-aortic lymphadenopathy, CT is 52% sensitive and 92% specific.

Chest CT could be obtained as a part of post-therapy surveillance in selected high-risk groups or patients with a higher FIGO stage; however, it is not needed for low-risk groups or patients with a lower FIGO stage, since pulmonary metastasis rarely occurs in the latter group. Performing chest

CT as an alternative to radiography for the initial diagnostic workup is controversial and still under investigation. However, it may be appropriate for high-risk and high-grade tumor confirmed by biopsy.

*Magnetic Resonance Imaging*

MRI is preferred over US or CT for pretreatment evaluation because it allows the most accurate evaluation of the extent of pelvic tumor. Evaluation of pelvic and para-aortic lymph nodes can be performed concurrently with accuracy comparable to CT with sensitivity of 44% to 66% and specificity of 73% to 98%. In addition, MRI is significantly superior to US in the evaluation of both tumor extension into the cervix and myometrial invasion. One study found that high-frequency transvaginal US has similar diagnostic accuracy in the evaluation of both tumor extension into the cervix (92% for high-frequency transvaginal US versus 85% for MRI) and myometrial invasion (84% for high-frequency transvaginal US versus 82% for MRI). A meta-analysis showed that the efficacy of contrast-enhanced MRI is significantly better than that of US, CT, or noncontrast MRI in evaluating the depth of myometrial invasion in patients with endometrial cancer.

*Dynamic Contrast-Enhanced Magnetic Resonance Imaging*

Multiple studies have demonstrated that dynamic contrast-enhanced MRI is a preferred modality to evaluate myometrial invasion with an accuracy, sensitivity, and specificity reaching as high as 100%. However, a great variation of these figures has been shown in different studies, ranging from 59% to 100% for accuracy, 71% to 100% for sensitivity, and 72% to 100% for specificity.

It has been clearly defined that T2-weighted imaging sequences alone have low sensitivity, specificity, and accuracy and should be combined with contrast-enhanced images. Dynamic contrast-enhanced MRI performs significantly better than unenhanced MRI for evaluating the depth of myometrial invasion, which is best demonstrated after 50 to 120 s postcontrast injection.

A negative finding on dynamic contrast-enhanced MR strongly suggests the absence of deep myometrial involvement. Superficial layers of the myometrium or junctional zone (JZ) typically enhance on arterial phase. Demonstration of an undisrupted enhancing JZ signifies lack of myometrial involvement. This is a useful sign to rule out a myometrial invasion in postmenopausal patients whose JZ is otherwise not well discernible on T2-weighted images.

Cervical extension can be diagnosed reliably with accuracy ranging from 86% to 95%. One study comparing MRI with fractional curettage and hysteroscopy showed that MRI had the highest sensitivity (91%) and specificity (96%) for diagnosing cervical involvement in endometrial cancer. Normal cervical stroma appears hypointense on T2-weighted images and provides an excellent contrast to the T2-weighted hyperintensity rendered by the tumoral invasion. Dynamic contrast-enhanced images (with a 180–240 s delay) further enhance the detection of such invasion. Studies have demonstrated accuracy up to 98% (range 46%–98%), sensitivity up to 100% (range 33%–100%), and specificity up to 100% (range 87%–100%).

The detection of pelvic lymphadenopathy according to size criteria (>10 mm in the shortest axis) has low sensitivity (17%–80%), high specificity (93%–100%), and moderate accuracy (83%–90%). Reducing the cut-off to 8 mm may further increase the sensitivity but decrease the specificity.

An erroneous MRI assessment of the depth of myometrial invasion can sometimes be ascribed to the presence of a large polypoid endometrial cancer, which distends the uterus so that a thin rim of myometrium is stretched over the polyp rather than cancer infiltration of the myometrium.

*Diffusion-Weighted Imaging and Apparent Diffusion Coefficient Mapping*

EC shows restricted diffusion and appears hyperintense on diffusion-weighted images (DWI) relative to surrounding myometrium. DWI has demonstrated very promising results in the assessment of deep myometrial invasion (accuracy 74%–98%, sensitivity 85%–100%, and specificity 82%–100%), especially when combined with T2-weighted imaging. These results are comparable to the contrast-enhanced MRI, thus DWI can be a potential alternative to patients with compromised kidney functions, where contrast is contraindicated.

On the other hand, ECs appear hypointense on apparent diffusion coefficient (ADC) maps, and an obvious difference of ADC values exists between benign and malignant endometrial lesions. This phenomenon has been exploited by certain investigators. With cut-off values $1.05 \times 10^{-3}$ $mm^2/s$ to differentiate benign from malignant tumors, the study results were highly encouraging (accuracy 95%, sensitivity 96%, and specificity 95%). Additionally, raising the cut-off value to 1.15 demonstrated an increased specificity (100%) but decreased sensitivity (85%).

DWI and ADC mapping may enhance the detection of metastatic lymph nodes in pelvic malignancies. Recently, it has been shown that metastatic nodes exhibit lower ADC values than the normal nodes, and minimum ADC region values are more reliable than the mean values to evaluate the suspicion of metastasis. With a cut-off value of $0.807 \times 10^{-3}$ $mm^2/s$, the sensitivity was 100%, specificity 98.3%, positive-predictive value 63.6%, negative-predictive value 100%, and accuracy 98.3%.

The role of DWI to determine tumor response to the treatment in EC is still evolving and not certain at press time.

MR perfusion and blood oxygen level dependent MRI do not have established roles in the evaluation of ECs. Certain ECs have demonstrated increased spectroscopic signals from choline, lipids, and lactates. This reaction could be exploited to determine long-term prognosis and treatment response on MR spectroscopy, but it needs validation. Magnetic iron oxide nanoparticles or ultra-small particles of iron oxides may demonstrate a potential in detecting malignant pelvic lymph nodes, but these particles are not widely available.

Studies have not shown any added advantage of using 3T versus 1.5T, and results are comparable for both 3T and 1.5T. However, 3T is more susceptible for susceptibility and chemical shift artifact, and image inhomogeneity of T2-weighted images were far inferior on 3T.

*Lymphangiography*

Lymphangiography is not recommended for evaluating cancer of the endometrium because 1) it is invasive, 2) few imaging centers offer this service, and 3) due to the difficulties of using it to evaluate pelvic nodes, its performance is not reproducible and is slightly inferior to that of CT and MRI, even when performed optimally.

*Positron Emission Tomography*

The role of positron emission tomography (PET) in endometrial cancer imaging is evolving. In detecting lymph node involvement by tumor, PET performs with accuracy (95%–98%) comparable to that of CT or MRI. However, because 45% of endometrial cancers are grade I and not fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-avid, the reported improved sensitivity of PET (60%–93%) is only true for nodes >1 cm. However, it has been shown that the sensitivity of FDG-PET alone or FDG-PET plus MRI-CT could be higher than that of MRI-CT alone in overall lesion detection. Higher FDG uptake or maximum standardized uptake value ($SUV_{max}$) of the primary tumors have been correlated with the higher recurrence rates. It has been shown that patients with high $SUV_{max}$ ($\geq$12.7) values had a significantly lower disease-survival rate. PET was reported to be useful in post-therapy surveillance for localizing suspected recurrences. A study showed that in the detection of recurrence and the evaluation of treatment response, FDG-PET, implemented by CT and/or MRI, performed better (sensitivity 100%, specificity 88.2%, and accuracy 93.3%) than CT and/or MRI (sensitivity 84.6%, specificity 85.7%, and accuracy 85%) and tumor markers, i.e., CA125, CA19-9, CEA, and sialyl TN antigen (sensitivity 100%, specificity 70.6%, and accuracy 83.3%). The results of FDG-PET correlated well with the clinical outcome of the patients; patients who had negative PET results tended to show disease-free courses.

*Radiography*

Chest radiography has traditionally been included as standard staging procedure after initial diagnosis of endometrial cancer. For imaging of patients at high risk for recurrence (i.e., high FIGO stage), radiography historically has represented an alternative to CT for chest imaging.

Summary

- Because dynamic contrast-enhanced and diffusion weighted MRI demonstrates the highest accuracy for overall staging of endometrial cancer, it should be the preferred imaging modality for treatment planning when available.
- Transvaginal US is still the screening examination of choice for the detection of EC, and it can be used to assess the depth of myometrial invasion and cervical involvement, albeit with less accuracy then MRI.
- CT and MRI perform equivalently for assessing nodal involvement. MRI might have an edge with ADC mapping.
- PET with concurrent diagnostic-quality abdominopelvic CT and/or MRI is the most accurate means of assessing adenopathy pretreatment and in the post-treatment evaluation of endometrial cancer patients with clinically suspected recurrence. However, cost-effectiveness or patient outcome analyses on the benefits of surveillance imaging have yet to be reported.
- Patients with endometrial cancer should undergo preoperative diagnostic imaging in cases where there is strong desire to preserve fertility or there are clinical staging difficulties, including medical comorbidities that preclude surgery, large tumors, high histologic tumor grade, or possible cervical involvement.
- Pretreatment imaging to determine tumor extent may be performed to plan surgery and, when necessary, triage to specialist referral for complete surgical staging with lymphadenectomy.
- If pretreatment imaging is needed, MRI is the preferred modality for overall assessment of disease extent. However, for the assessment of lymphadenopathy and distant metastasis, CT is also acceptable. However, PET/CT is more appropriate for assessing lymphadenopathy in high-grade FDG-avid tumors.
- For clinically suspected recurrence after treatment, PET/CT is the preferred imaging modality to confirm and localize the recurrent disease. There is not enough evidence to support post-therapy imaging surveillance for asymptomatic patients at this time.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based

contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 $m^2$), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 $m^2$. For more information, see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Abbreviations

- CT, computed tomography
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography
- MRI, magnetic resonance imaging
- US, ultrasound

Relative Radiation Level Designations

| Relative Radiation Level* | Adult Effective Dose Estimate Range | Pediatric Effective Dose Estimate Range |
|---|---|---|
| O | 0 mSv | 0 mSv |
| | <0.1 mSv | <0.03 mSv |
| | 0.1-1 mSv | 0.03-0.3 mSv |
| | 1-10 mSv | 0.3-3 mSv |
| | 10-30 mSv | 3-10 mSv |
| | 30-100 mSv | 10-30 mSv |
| *RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies." | | |

## Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

# Scope

## Disease/Condition(s)

Endometrial cancer

## Guideline Category

Evaluation

Risk Assessment

## Clinical Specialty

Family Practice

Internal Medicine

Nuclear Medicine

Obstetrics and Gynecology

Oncology

Radiology

Surgery

## Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

## Guideline Objective(s)

To evaluate the appropriateness of radiologic examinations for the pretreatment evaluation and follow-up of endometrial cancer

## Target Population

Women with endometrial cancer

## Interventions and Practices Considered

1. Magnetic resonance imaging (MRI)
    - Pelvis without and with contrast
    - Pelvis without contrast
    - Abdomen without contrast
    - Abdomen without and with contrast
2. X-ray chest
3. Computed tomography (CT)
    - Chest with contrast
    - Chest without contrast
    - Chest without and with contrast
    - Pelvis with contrast
    - Pelvis without contrast
    - Pelvis without and with contrast
    - Abdomen with contrast
    - Abdomen without contrast
    - Abdomen without and with contrast
4. Ultrasound (US)
    - Pelvis transvaginal
    - Saline infusion sonohysterography
    - Pelvis transabdominal
5. Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET)/CT skull base to mid-thigh
6. Lymphangiogram (not recommended)

## Major Outcomes Considered

Utility of radiologic examinations in pretreatment evaluation and follow-up of endometrial cancer

# Methodology

## Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

Staff will search in PubMed only for peer reviewed medical literature for routine searches. Any article or guideline may be used by the author in the narrative but those materials may have been identified outside of the routine literature search process.

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches.

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 10 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

## Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Strength of Evidence Key

Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.

Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.

Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.

Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence (study quality) for each article included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

## Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

## Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distribute surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The appropriateness rating scale is an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate"; 4, 5, or 6 are in the category "may be appropriate"; and 7, 8, or 9 are in the category "usually appropriate." Each panel member assigns one rating for each procedure for a clinical scenario. The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating.

If consensus is reached, the median rating is assigned as the panel's final recommendation/rating. Consensus is defined as eighty percent (80%) agreement within a rating category. A maximum of three rounds may be conducted to reach consensus. Consensus among the panel members must be achieved to determine the final rating for each procedure.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is proposed as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

This modified Delphi method enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive influence from fellow panelists in a simple, standardized and economical process. A more detailed explanation of the complete process can be found in additional methodology documents found on the ACR Web site (see also the "Availability of Companion Documents" field).

## Rating Scheme for the Strength of the Recommendations

Not applicable

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Internal Peer Review

## Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

# Evidence Supporting the Recommendations

## Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

# Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

Selection of appropriate radiologic imaging procedures for the pretreatment evaluation and follow-up of endometrial cancer

## Potential Harms

Hysterosonography (transvaginal ultrasound evaluation of the uterus after intracavitary saline infusion) has been used for evaluating deep myometrial invasion, with accuracies ranging from 84% to 89%; however, its use is controversial in determining the myometrial invasion, and several reports indicated that the procedure can disseminate malignant cells into the peritoneal cavity in 6% to 7% of patients with an established diagnosis of endometrial cancer.

Gadolinium-Based Contrast Agents

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 $m^2$), and almost never in other patients. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 $m^2$. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Relative Radiation Level (RRL)

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR)

Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

# Qualifying Statements

## Qualifying Statements

### Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Living with Illness

## IOM Domain

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

Lalwani N, Dubinsky T, Javitt MC, Gaffney DK, Glanc P, Elshaikh MA, Kim YB, Lee LJ, Pannu HK, Royal HD, Shipp TD, Siegel CL, Simpson L, Wahl AO, Wolfson AH, Zelop CM, Expert Panel on Women's Imaging and Radiation Oncology â€“ Gynecology. ACR Appropriateness CriteriaÂ® pretreatment evaluation and follow-up of endometrial cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 12 p. [61 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

1999 (revised 2013)

## Guideline Developer(s)

American College of Radiology - Medical Specialty Society

## Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

## Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Women's Imaging and Radiation Oncology – Gynecology

## Composition of Group That Authored the Guideline

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## Financial Disclosures/Conflicts of Interest

Not stated

## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Lee J, Dubinsky T, Andreotti RF, Cardenes HR, Allison SO, Gaffney DK, Glanc P, Horowitz NS, Jhingran A, Lee SI, Puthawala AA, Royal HD, Scoutt LM, Small W Jr, Varia MA, Zelop CM, Expert Panel on Women's Imaging and Radiation Oncology - Gynecology. ACR Appropriateness Criteria® pretreatment evaluation and follow-up of endometrial cancer of the uterus. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 9 p.

## Guideline Availability

Electronic copies: Available from the American College of Radiology (ACR) Web site .

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

## Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site .

- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – therapeutic studies. Reston (VA): American College of Radiology; 2013 Nov. 4 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 90 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available in PDF from the ACR Web site.
- ACR Appropriateness Criteria® pretreatment evaluation and follow-up of endometrial cancer. Evidence table. Reston (VA): American College of Radiology; 2013. 22 p. Electronic copies: Available from the ACR Web site.

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI on February 10, 2006. This NGC summary was updated by ECRI Institute on August 10, 2009. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on July 29, 2011. This NGC summary was updated by ECRI Institute on March 12, 2014.

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